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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,787	05/04/2005	Yannis Tsouderos	SERVIER 455 PCT	4570

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EXAMINER	
ROGERS, JUNE MARIE	
ART UNIT	**PAPER NUMBER**
1612	

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05/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,787	TSOUDEROS, YANNIS	
	Examiner	Art Unit	
	JUNE ROGERS	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/14/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Previous Rejections

Unless specifically repeated/maintained **infra**, all previous rejections are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of gastro-duodenal pain, does not reasonably provide enablement treatment of gastritis or doudenitis (forms of inflammation). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to In re Wands, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing Ex parte Forman, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those

in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention:

The instant invention relates the treatment gastro-duodenal pain by administration of the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4- carboxymethyl-thiophene-5-carboxylic acid or hydrates thereof.

The relative skill of those in the art:

The relative skill of those in the art is high, with a typical practitioner having obtained a MD, PhD, M.S. or equivalent advanced degree.

The breadth of the claims

The instant claims are deemed very broad since "gastritis and/or duodenitis" is not are single conditions rather they generically refer to different conditions that all have inflammation of the stomach lining, in the case of gastritis or duodenum, in the case of doudenitis.

The predictability or lack thereof in the art and the amount of direction or guidance presented:

In the instant case, the instant claimed invention is highly unpredictable. See "The inflammatory reflex" Nature (2002) vol. 420 19/26.

As such, the efficacy of the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4- carboxymethyl-thiophene-5-carboxylic acid will need to be individually evaluated in the treatment of such inflammation.

The specification, as filed, fails to enable one of skill in the art to use the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4- carboxymethyl-thiophene-5-carboxylic acid or hydrates thereof for the treatment gastritis or doudenitis. For example, the Applicant provides data from clinical study. However, not a single example of the type of condition being treated is provided in the specification, what is being treated (i.e., is it the pain or the inflammation associated with said conditions). Such is the case for most of Applicant's generic descriptors. One of skill in the art will recognize that in order use the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4- carboxymethyl-thiophene-5-carboxylic acid for the treatment of gastritis or doudenitis a substantial research and development effort is needed.

The presence or absence of working examples the quantity of experimentation necessary:

Applicant provides no examples of the treatment of gastritis or doudenitis. . Applicant's data is insufficient to ascertain, the patient population i.e. was this study done in human or animals and whether or not the difference reported was significant. Furthermore, the art does not recognize the treatment of gastritis or duodenitis with the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4- carboxymethyl-thiophene-5-carboxylic acid. This compound is typically used to treat osteoporosis. Applicant has failed to demonstrate that the distrontium salt of 2-[N,N-di(carboxymethyl)amino]-3-cyano-4- carboxymethyl-thiophene-5-carboxylic acid can be used for the treatment of gastritis of doudenitis. There are no conditions shown to be treated with said compound.

Therefore, in view of the Wands factors as discussed above, to practice the claimed invention herein, a person of skill in the art would not be able to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Lacharriere et al. (USP 5,866,168) in view of Wierzbickl et al. (USP 5,128,367).

For the purpose of applying art, Examiner is interpreting Applicant's recitation of gastritis and/or duodenitis as referring to treating the pain associated with these conditions and not the inflammation associated with said conditions.

The primary reference teaches the use of strontium salts for the treatment of diseases which respond P antagonism. It differs from the instant claims insofar as it does not teach thiophene compound.

Lacharriere et al teaches that substance P is involved, in particular, in the transmission of pain (col. 1, 37-38) and in diseases such as gastrointestinal diseases (such as , gastritis, gastroenteritis etc.). Lacharriere et al. further teaches substance P antagonist have been administered to treat gastrointestinal diseases (col. 2, lines 15-16). Lacharriere et al. discloses that strontium salts are substances P antagonist. (col. 2, lines 33-35).

Wierzbickl et al. teaches that thiophene compound is pharmaceutically useful and is highly desirable because it provides bioavailability (column 2, lines 32-38). It differs insofar as it does not specifically teach treating GI.

Accordingly, it would have been obvious to one of ordinary skill in the art to treat pain that is associated with substance P (i.e. gastritis/deuodentis) with the divalent strontium salt (i.e. strontium renalate), which is a known substance P antagonist. One of ordinary skill in the art would be motivated to do so because one would recognize that any substance P antagonist would have the ability to treat pain in a condition in which substance P was involved in the transmission of pain. In particular, one would be motivated to use the divalent salt of the instantly claimed thiopene compound because the divalent salts of said compounds are known to have improved bioavailability.

Conclusion

No claims allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to JUNE ROGERS whose telephone number is (571)270-3497. The examiner can normally be reached on M-F 9-6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fred Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Juné M. Rogers

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612